IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Michael A. Tainsky, et al. Confirmation No.: 5172

Serial No.: 10/004,587 Group Art Unit: 1631

Filed: 12/04/2001 Examiner: CLOW, Lori A.

For: NEOEPITOPE DETECTION OF DISEASE USING PROTEIN ARRAYS

Attorney Docket No.: 0788.00063

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION

I, Dr. Michael A. Tainsky, being duly sworn, do hereby state that:

1. I am a co-inventor of the above-captioned application.

2. I am skilled in the art and have worked extensively in the field of biopanning and cancer detection.

3. Sioud, et al. is cited in combination with either Miller, et al. or Robinson, et al. against presently pending claim 20 as being unpatentable under 35 U.S.C. §103(b). It is respectfully submitted herein that the present invention provides unexpected results and is patentable over the cited prior art.

More specifically, it is undisputed that the primary reference, the Sioud, et al., reference, discloses the step of biopanning libraries for selecting phage display cDNA products recognized by a significant number of breast cancer sera as compared to sera from normal individuals. The Sioud, et al., reference concluded that "the obtained results demonstrate that phage display could be a valuable method for the identification of antigens recognized by the humoral immune system in patients with cancer." (Sioud, et al., reference, abstract).

It is admitted that it is well-known to biopan for a specific composition, as disclosed in the Sioud, et al. reference. That is, the Sioud, et al., reference discloses biopanning methods aimed at determining the presence of a single significant marker. There is no disclosure in the Sioud, et al. reference of a method or assay that simultaneously screens for an unlimited number of markers within

sera. The cited reference only teaches obtaining approximately five to ten markers. This is known in the art to be a low throughput method. This is consistent with the commonly accepted convention of determining a single marker for diagnostic purposes, such as those used for prostate cancer, breast cancer, or the like. Moreover, the methodology disclosed in the Sioud, et al., reference teaches away from the use of a large array, or more specifically, including all epitopes uncovered during biopanning related to a disease, because the primary goal, as disclosed in the first full paragraph of page 718 of the Sioud, et al., reference is to ". . . enrich for the best binders. If the selection is specific an increase in the number of positive clones is likely."

"[It is an] error to find obviousness where references 'diverge from and teach away from the invention at hand'". *In re Fine*, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988) (citing *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550, 220 USPQ 303, 311 (Fed. Cir. 1983)).

The additional selections disclosed in the Sioud, et al., reference were designed to increase the specificity for finding a few highly specific markers. Identifying ***all*** epitopes in the present invention and therefore requiring a large protein array is certainly not the same as identifying ***five to ten*** markers as in Sioud, et al. Certainly, if five to ten markers are sufficient to detect cancer according to Sioud, et al., there is no reason to use a microarray to obtain markers.

"If, however, the examiner does produce a prima facie case, the burden of coming forward with evidence or arguments shifts to the applicant who may submit additional evidence of nonobviousness, such as comparative test data showing that the claimed invention possesses improved properties not expected by the prior art." MPEP 2142 (2100-127).

The present invention provides unexpected results in view of the convention of the prior art. The present invention, as set forth in independent claim 20, is characterized by identifying ***all epitope-bearing clones*** that are specific to early-stage cancer and including ***all epitopes identified*** in protein arrays for detecting early-stage cancer. This teaching goes directly against the teachings of the cited prior art. Moreover, the present invention as set forth in pending claim 20 provides

unexpected results by providing a broad range, yet sensitive assay, capable of detecting early-stage cancer, as supported on page 42 of the presently pending patent application. The present invention provides a method of identifying and detecting markers indicative of early-stage cancer, thereby allowing the practitioner to utilize more specific diagnostic procedures to confirm the early-stage cancer and then prescribe early-stage treatments. The prior art does not provide markers nor does it even suggest the provision of markers for such early-stage detection of cancer. Treatment of early-stage cancer is known to be significantly more effective than treatment of later-stage cancer. Choosing only a few markers in Sioud, et al. through low throughput approaches would be insensitive, i.e. many false negatives would be detected among cancer bearing test subjects. Hence, the present invention provides unexpected results not obtained by the prior art. That is, the present invention includes all epitopes identified in protein array assays for detecting early-stage cancer. Such unexpected results overcome a *prima facie* obviousness-type rejection as a matter of law. Hence, it is respectfully submitted that independent claim 20 is patentable over the cited prior art.

The undersigned declares further all statements made herein of his knowledge are true and that all statements made upon information and belief are believed to be true, and further that the statements were made with the knowledge that willful and false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: June 4, 2008

Dr. Michael A. Tainsky